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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,514	12/11/2003	Daniel A. Moros	03939/100M269-US1	1588

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TARO PHARMACEUTICALS U.S.A., INC.
C/O VENABLE LLP
P.O. BOX 34385
WASHINGTON, DC 20045-9998

EXAMINER	
OLSON, ERIC	
ART UNIT	**PAPER NUMBER**
1623	

DATE MAILED: 08/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/735,514	MOROS, DANIEL A.	
	Examiner	Art Unit	
	Eric S. Olson	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *December 11, 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *38-40,50-52,59 and 60* is/are allowed.

6)☒ Claim(s) *1-30,36,37,41,42,48,49,and 53-57* is/are rejected.

7)☒ Claim(s) *31-35,43-47 and 58* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/24/04, 7/15/04*. 7/26/04
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

This application claims benefit of provisional application 60/432470, filed December 11, 2002. Claims 1-60 are pending in this application and examined on the merits herein. Applicant's preliminary amendment submitted July 9, 2004 is acknowledged wherein claim 59 is amended.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 10-20, 23-28, and 53-57 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating tremors associated with essential tremor or Parkinson's disease, does not reasonably provide enablement for a method of treating other movement disorders such as dystonias. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The Applicant's attention is drawn to *In re Wands*, 8 USPQ2d 1400 (CAFC1988) at 1404 where the court set forth eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) The nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The claimed invention is a method of treating movement disorders by administering a compound of a formula disclosed in instant claim 1.

The state of the prior art: It is known in the prior art that the various movement disorders, although all deriving form neurological causes, differ significantly in causes, effects, and treatment. Therapies effective for one movement disorder are not necessarily effective against another movement disorder. For example, according to the Merck manual of diagnosis and therapy, seventeenth edition, (reference included with PTO-892) tremors usually respond to benzodiazepines, propranolol, or primidone. (p. 1463, left column, last paragraph, right column, first paragraph) Huntington's Chorea, on the other hand, is not effectively treatable, with only partial symptomatic relief being provided by antipsyschotcs. (p. 1465, left column, last paragraph) Treatment of dystonias is also often unsatisfactory, with injections of botulinum toxin providing some relief for focal dystonia. (p. 1466, left column)

Some compounds of the disclosed structure, such as phenobarbitol, are known in the prior art to be useful for the treatment of essential tremor and movement disorders associated with Parkinson's disease. They are not known to be useful for the treatment of movement disorders generally.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or unpredictability of the art: As mentioned above, different movement disorders do not respond to the same therapies. Merely being effective against one particular movement disorder, such as essential tremor, does not indicate that a therapy is effective against all movement disorders. Thus the treatment of movement disorders is an unpredictable art.

The Breadth of the claims: The instant claims include methods of treating any movement disorder by administering a therapeutic active agent. Disorders to be treated include, but are not limited to, essential tremor, Parkinson's disease, focal and generalized dystonia, Huntington's Chorea, and extrapyrimidal symptoms caused by antipsychotic drugs.

The amount of direction or guidance presented: Applicant's specification provides guidance for methods of synthesizing the disclosed therapeutic agents and for suggested dosage forms. Applicant's specification speculates that these compounds are useful for the treatment of movement disorders but does not give any specific reasons for expecting such a broad therapeutic utility.

The presence or absence of working examples: One working example is provided of a human trial demonstrating the effectiveness of the claimed therapeutic method in the treatment of essential tremor. Two other possible human trials are described, but these descriptions are merely speculative and do not disclose actual experimental results.

Note that lack of working examples is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the generalized treatment of movement disorders. See MPEP 2164.

The quantity of experimentation necessary: In order to practice the claimed invention for the treatment of all movement disorders, one skilled in the art would be required to test the disclosed compounds in appropriate models of these disorders.

Because this class of disorders is complex, multiple models would be needed, either in animals or humans. Animal experiments involve, along with the actual experimentation, additional burdens associated with the care and feeding of animals, compliance with ethical and regulatory requirements, and disposal of dead animals after the experiment is complete. Human experiments involve greater ethical and regulatory burdens, as well as the burden of recruiting subjects. Performing these experiments for the disclosed compounds for every distinct class of movement disorders, with no guidance from Applicant's disclosure or reasonable expectation of success, represents an undue experimental burden in order to practice the claimed invention.

Genentech, 108 F.3d at 1366, sates that, "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion." And "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

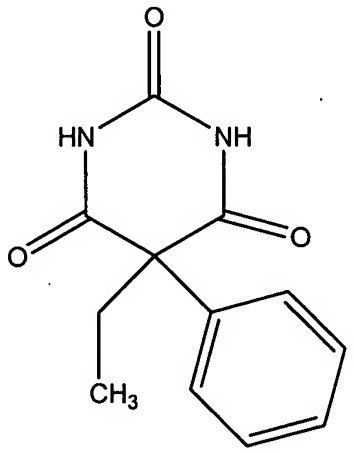
Therefore, in view of the Wands factors, as discussed above, particularly the breadth of the claims and the lack of precedent in the prior art, Applicants fail to provide

information sufficient to practice the claimed invention for the treatment of all movement disorders.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 14, 15, 21, 27, 14, 29, 30, and 53 are rejected under 35 U.S.C. 102(b) as being anticipated by Sasso et al. (Reference included with PTO-1449) Sasso et al. discloses a method of treating essential tremor by administering phenobarbital, an embodiment of the structure disclosed in instant claim 1: (p. 65, right column, p. 66, left column)



Phenobarbital was administered in tablet form in a dose gradually escalating according to tolerability, to a maximum dose of three 50 mg tablets per day. This method is a method of treating essential tremor comprising administering to a subject in need of treatment a composition comprising an amount effective for this purpose of a

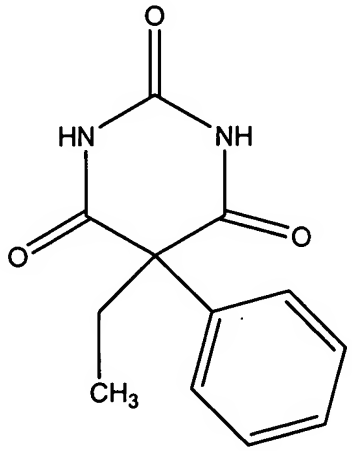
compound according to the formula disclosed in instant claim 1. Sasso et al. therefore anticipates the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12, 13, 25, 26, 36, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sasso et al. (Reference included with PTO-1449) Sasso et al. discloses a method of treating essential tremor by administering phenobarbital, an embodiment of the structure disclosed in instant claim 1: (p. 65, right column, p. 66, left column)



Phenobarbital was administered in tablet form in a dose gradually escalating according to tolerability, to a maximum dose of three 50 mg tablets per day.

This method is a method of treating essential tremor comprising administering to a subject in need of treatment a composition comprising an amount effective for this purpose of a compound according to the formula disclosed in instant claim 1. Sasso et al. does not disclose such a method comprising administering the compound in a dose of 150-1500 or 200-1200mg as disclosed by instant claims 12, 13, 25, 26, 36, 37.

It would have been obvious to one of ordinary skill in the art at the time of the invention to practice the method of Sasso et al. with a dose of 150-1500 or 200-1200 mg of the active agent. One of ordinary skill in the art would have been motivated to use this dose because the disclosed dose of 150 mg is at one end of the claimed range of instant claims 12, 25, and 36, and is very close to falling within the range of instant claims 13, 26, and 37. One of ordinary skill in the art would reasonably have expected success because determining the specific optimal dosage amount is well within the routine skill of one of ordinary skill in the art.

Thus the invention taken as a whole is *prima facie* obvious.

Claims 1, 2, 9, 12-15, 22, 25-30, 36-37, 41, 42, 48, 49, and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curry (Reference included with PTO-1449) Curry discloses a number of barbiturate derivatives. (p. 5) Certain embodiments of these derivatives, in which R1 and R2 are $(CH_2)_nCR5H_2$, R5 is alkyl, and R3 and R4 are hydrogen fall within the limits of the structures disclosed in instant claims 1 and 2. These compounds are disclosed to be useful for the treatment of disorders including movement disorders associated with Parkinson's disease. (p. 4, second paragraph) The

suggested dosage at which the therapeutic agents are to be administered is, in an especially preferred embodiment, between 0.1 and 15 mg/kg/day, or between 7 and 1050 mg/day for a 70kg patient. (p. 27, line 2) Specific pharmaceutical dosage forms include tablets, gelatin capsules, aerosols, suppositories, suspensions, and intravenous and topical formulations. Curry does not specifically disclose a method of treating movement disorders associated with Parkinson's disease by administering the specific embodiment described above. Curry also does not specifically disclose such a method involving administering the compound at a dose of between 150 and 1500 or 200 and 1200 mg/day in a divided dose.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the invention of Curry to treat movement disorders associated with Parkinson's disease by administering a compound according to the generic formula disclosed by Curry in which R1 and R2 are $(CH_2)_nCR5H_2$, R5 is alkyl, and R3 and R4 are hydrogen. It would also have been obvious to administer this compound in a divided dose of 200-1000 mg/day. One of ordinary skill in the art would have been motivated to use a compound of this specific formula because these compounds fall within the generic structure disclosed by Curry. One of ordinary skill in the art would have been motivated to administer a divided dose of 200-1000 mg/day because this dose falls within the dose range disclosed by Curry. When the claimed ranges, "overlap or lie inside ranges disclosed by the prior art," a prima facie case of obvious exists. See *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976); *In re Woodruff*, 919 F.2d 1575, 16 USPQ2d 1934 (Fed. Cir. 1990). See MPEP 2144.05 [R-1]. One of ordinary

skill in the art would have reasonably expected success because these modifications are within the scope revealed to be useful by Curry's disclosure.

Thus the invention taken as a whole is *prima facie* obvious.

Claim Objections

Claims 31-35, 43-47, and 58 are objected to as depending from rejected base claims but would be allowable if rewritten in independent form incorporating all the limitations of the base claim and all intervening claims.

Allowable Subject Matter

The claimed methods of treating essential tremor and Parkinson's disease comprising administering a diphenylbarbituate compound as claimed by claims 38-40, 50-52, and 59-60 are seen to be novel and non-obvious over the prior art and are directed to subject matter adequately described and enabled by Applicant's specification. For example, written description and enablement are provided by the *in vivo* therapeutic method and experimental data disclosed on pp. 28-31 of Applicant's specification. The specific structures claimed by the indicated claims are not known in the prior art to be useful for the treatment of movement disorders, and no methods of treating movement disorders by administering these compounds have been disclosed in the prior art. The diphenyl- and mono-or di- methoxymethyl- derivatives of the disclosed structure are non-obvious over the prior art compounds known to be useful for treating

movement disorders, such as phenobarbital. Therefore the indicated subject matter is allowable.

Summary

Claims 1-30, 36, 37, 41, 42, 48, 49, and 53-57 are rejected. Claims 38-40, 50-52, and 59-60 are found to be in condition for allowance. Claims 31-35, 43-47, and 58 are objected to as depending from rejected base claims but would be allowable if rewritten in independent form incorporating all the limitations of the base claim and all intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric Olson
Patent Examiner
AU 1623
8/16/06

Anna Jiang
Supervisory Patent Examiner
AU 1623